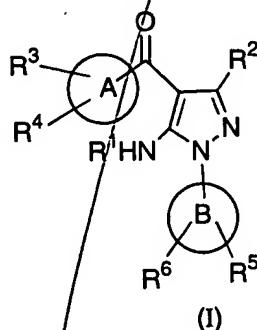


**What is Claimed:**

1. A compound selected from the group of compounds represented by Formula (I):



wherein:

R<sup>1</sup> is hydrogen or acyl;

R<sup>2</sup> is hydrogen or alkyl;

A is an aryl or heteroaryl ring;

B is an aryl or heteroaryl ring;

R<sup>3</sup> is selected from the group consisting of:

- (a) amino, alkylamino or dialkylamino;
- (b) acylamino;
- (c) optionally substituted heterocyclyl;
- (d) optionally substituted aryl or heteroaryl;
- (e) heteroalkyl;
- (f) heteroalkenyl;
- (g) heteroalkynyl;
- (h) heteroalkoxy;
- (i) heteroalkylamino;
- (j) optionally substituted heterocyclylalkyl;
- (k) optionally substituted heterocyclylalkenyl;
- (l) optionally substituted heterocyclylalkynyl;
- (m) optionally substituted heterocyclylalkoxy, cyclyloxy or heterocyclloxy;

- (n) optionally substituted heterocyclalkylamino;
- (o) optionally substituted heterocyclalkylcarbonyl;
- (p) heteroalkylcarbonyl;
- (q)  $\text{-NHSO}_2\text{R}^6$  where  $\text{R}^6$  is alkyl, heteroalkyl or optionally substituted heterocyclalkyl;
- (r)  $\text{-NHSO}_2\text{NR}^7\text{R}^8$  where  $\text{R}^7$  and  $\text{R}^8$  are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (s)  $\text{-Y-(alkylene)-R}^9$  where:  
 Y is a single bond,  $\text{-O-}$ ,  $\text{-NH-}$  or  $\text{-S(O)}_n\text{-}$  (where n is an integer from 0 to 2); and  
 $\text{R}^9$  is cyano, optionally substituted heteroaryl,  $\text{-COOH}$ ,  $\text{-COR}^{10}$ ,  $\text{-COOR}^{11}$ ,  $\text{-CONR}^{12}\text{R}^{13}$ ,  $\text{-SO}_2\text{R}^{14}$ ,  $\text{-SO}_2\text{NR}^{15}\text{R}^{16}$ ,  $\text{-NHSO}_2\text{R}^{17}$  or  $\text{-NHSO}_2\text{NR}^{18}\text{R}^{19}$ , where  $\text{R}^{10}$  is alkyl or optionally substituted heterocycle,  $\text{R}^{11}$  is alkyl, and  $\text{R}^{12}$ ,  $\text{R}^{13}$ ,  $\text{R}^{14}$ ,  $\text{R}^{15}$ ,  $\text{R}^{16}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$  and  $\text{R}^{19}$  are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (t)  $\text{-C(=NR}^{20}\text{)(NR}^{21}\text{R}^{22}\text{)}$  where  $\text{R}^{20}$ ,  $\text{R}^{21}$  and  $\text{R}^{22}$  independently represent hydrogen, alkyl or hydroxy, or  $\text{R}^{20}$  and  $\text{R}^{21}$  together are  $\text{-(CH}_2\text{)}_n\text{-}$  where n is 2 or 3 and  $\text{R}^{22}$  is hydrogen or alkyl;
- (u)  $\text{-NHC(X)NR}^{23}\text{R}^{24}$  where X is  $\text{-O-}$  or  $\text{-S-}$ , and  $\text{R}^{23}$  and  $\text{R}^{24}$  are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (v)  $\text{-CONR}^{25}\text{R}^{26}$  where  $\text{R}^{25}$  and  $\text{R}^{26}$  independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclalkyl, or  $\text{R}^{25}$  and  $\text{R}^{26}$  together with the nitrogen to which they are attached form an optionally substituted heterocycl ring;
- (w)  $\text{-S(O)}_n\text{R}^{27}$  where n is an integer from 0 to 2, and  $\text{R}^{27}$  is alkyl, heteroalkyl, optionally substituted heterocyclalkyl or

-NR<sup>28</sup>R<sup>29</sup> where R<sup>28</sup> and R<sup>29</sup> are, independently of each other, hydrogen, alkyl or heteroalkyl;

- (x) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (y) arylaminoalkylene or heteroarylaminomethylene;
- (z) Z-alkylene-NR<sup>30</sup>R<sup>31</sup> or Z-alkylene-OR<sup>32</sup> where Z is -NH-, -N(lower alkyl)- or -O-, and R<sup>30</sup>, R<sup>31</sup> and R<sup>32</sup> are independently of each other, hydrogen, alkyl or heteroalkyl;
- (aa) -OC(O)-alkylene-CO<sub>2</sub>H or -OC(O)-NR'R'' (where R' and R'' are independently hydrogen or alkyl); and
- (bb) heteroarylalkenylene or heteroarylalkynylene;

R<sup>4</sup> is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R<sup>5</sup> is selected from the group consisting of :

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;

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- (m) optionally substituted heterocyclalkoxy;
  - (n) alkylsulfonyl;
  - (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
  - (p) heteroalkoxy; and
  - (q) carboxy;

R<sup>6</sup> is selected from the group consisting of:

- 10
- (a) hydrogen;
  - (b) halo;
  - (c) alkyl; and
  - (d) alkoxy;

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

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The compound of Claim 1 wherein R<sup>3</sup> is:

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- (a) optionally substituted heterocycl;
  - (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO<sub>2</sub>R' (where R' is alkyl) or SO<sub>2</sub>NHR'R'' (where R' and R'' are independently hydrogen or alkyl);
  - (c) heteroalkyl;
  - (d) heteroalkenyl;
  - (e) heteroalkylamino;
  - (f) heteroalkoxy;
  - (g) optionally substituted heterocyclalkyl or heterocyclalkoxy;
  - (h) optionally substituted heterocyclalkenyl;
  - (i) optionally substituted heterocyclalkynyl;
  - (j) optionally substituted heterocyclalkoxy;
  - (k) optionally substituted heterocyclalkylamino;
  - (l) optionally substituted heterocyclalkylcarbonyl;
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- (k) -Y-(alkylene)-R<sup>9</sup> where Y is a single bond, -O- or -NH- and R<sup>9</sup> is optionally substituted heteroaryl, -CONR<sup>12</sup>R<sup>13</sup>, SO<sub>2</sub>R<sup>14</sup>, -SO<sub>2</sub>NR<sup>15</sup>R<sup>16</sup>, -NHSO<sub>2</sub>R<sup>17</sup> or -NHSO<sub>2</sub>NR<sup>18</sup>R<sup>19</sup> where R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup> are independently of each other hydrogen, alkyl or heteroalkyl;
- (l) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (m) arylaminoalkylene or heteroarylaminomethylene; or
- (n) Z-alkylene-NR<sup>30</sup>R<sup>31</sup> where Z is -NH-, -N(alkyl)- or -O-, and R<sup>30</sup> and R<sup>31</sup> are independently of each other, hydrogen, alkyl or heteroalkyl.

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3. The compound of Claim 2 wherein R<sup>1</sup> and R<sup>2</sup> are hydrogen; and B is phenyl.
4. The compound of Claim 3 wherein A is phenyl.
5. The compound of Claim 4 wherein R<sup>4</sup> is hydrogen; and R<sup>5</sup> is halo or alkyl.
6. The compound of Claim 5 wherein R<sup>5</sup> is chloro, fluoro or methyl; and R<sup>6</sup> is hydrogen, chloro, fluoro, methyl or methoxy.
7. The compound of Claim 5, wherein R<sup>3</sup> is optionally substituted heteroaryl.
8. The compound of Claim 7, wherein R<sup>3</sup> is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
9. The compound of Claim 8, wherein R<sup>3</sup> is at the 3-position.
10. The compound of Claim 9, wherein R<sup>5</sup> is 4-F and R<sup>6</sup> is hydrogen.
11. The compound of Claim 9, wherein R<sup>5</sup> is 2-Me and R<sup>6</sup> is hydrogen.

12. The compound of Claim 5, wherein  $R^3$  is optionally substituted phenyl.

13. The compound of Claim 12, wherein  $R^3$  is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

14. The compound of Claim 13, wherein  $R^3$  is at the 3-position.

15. The compound of Claim 14, wherein  $R^5$  is 4-F and  $R^6$  is hydrogen.

16. The compound of Claim 5, wherein  $R^3$  is:

- (a) heteroalkyl;
- (b) heteroalkoxy;
- (c) heteroalkylamino;
- (d) optionally substituted heterocyclalkyl;
- (e) optionally substituted heterocyclalkoxy;
- (f) optionally substituted heterocyclalkylamino;
- (g)  $-Y-(alkylene)-R^9$  where Y is a single bond, -O- or -NH- and  $R^9$  is optionally substituted heteroaryl,  $-CONR^{12}R^{13}$ ,  $SO_2R^{14}$ ,  $-SO_2NR^{15}R^{16}$ ,  $NHSO_2R^{17}$  or  $-NHSO_2NR^{18}R^{19}$  where  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$  and  $R^{19}$  are independently of each other hydrogen, alkyl or heteroalkyl; or
- (h)  $Z-alkylene-NR^{30}R^{31}$  where Z is -NH-, -N(alkyl)- or -O-, and  $R^{30}$  and  $R^{31}$  are independently of each other, hydrogen, alkyl or heteroalkyl.

17. The compound of Claim 16, wherein  $R^3$  is heteroalkyl.

18. The compound of Claim 17, wherein  $R^3$  is at the 3-position and is selected from the group consisting of 2-dimethylaminoethyl, 3-dimethylaminopropyl, 4-dimethylaminobutyl, 2-dimethylaminoethylamino, 3-dimethylaminopropylamino, hydroxymethyl, 1,2-dihydroxyethyl, 3-hydroxy-3-methyl-1-butyl or 3-hydroxybutyl.

19. The compound of Claim 18, wherein R<sup>5</sup> is 2-F and R<sup>6</sup> is 4-F.
20. The compound of Claim 18, wherein R<sup>5</sup> is 4-F and R<sup>6</sup> is hydrogen.
- 5 21. The compound of Claim 18, wherein R<sup>5</sup> is 2-Me and R<sup>6</sup> is hydrogen.
22. The compound of Claim 16, wherein R<sup>3</sup> is heteroalkoxy or heteroalkylamino.
23. The compound of Claim 22, wherein R<sup>3</sup> is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, 2-dimethylaminoethylamino and 3-dimethylaminopropylamino.
24. The compound of Claim 23 wherein R<sup>5</sup> is 4-F or 2-Me and R<sup>6</sup> is hydrogen.
- 15 25. The compound of Claim 16, wherein R<sup>3</sup> is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.
- 20 26. The compound of Claim 25, wherein R<sup>3</sup> is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxypiperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.
- 25 27. The compound of Claim 26 wherein R<sup>5</sup> is 4-F or 2-Me and R<sup>6</sup> is hydrogen.

28. The compound of Claim 16 wherein  $R^3$  is  $-Y-(alkylene)-R^9$  where Y is a single bond, -O- or -NH- and  $R^9$  is optionally substituted heteroaryl,  $-CONR^{12}R^{13}$ ,  $SO_2R^{14}$ ,  $SO_2NR^{15}R^{16}$ ,  $-NHSO_2R^{17}$  or  $-NHSO_2NR^{18}R^{19}$  where  $R^{12}$ ,  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$  and  $R^{19}$  are independently of each other hydrogen, alkyl or heteroalkyl.

29. The compound of Claim 28, wherein Y is a single bond and  $R^9$  is  $SO_2R^{14}$  or  $SO_2NR^{15}R^{16}$ .

30. The compound of Claim 29 wherein  $R^3$  is methylsulfonylethyl or sulfamoylethyl.

31. The compound of Claim 30 wherein  $R^5$  is 4-F or 2-Me and  $R^6$  is hydrogen.

32. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable excipient.

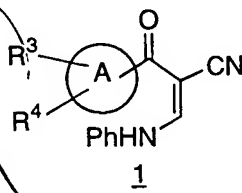
33. A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound of Claim 1.

34. The method of Claim 33 wherein the disease is an inflammatory disease.

35. The method of Claim 34 wherein the disease is arthritis.

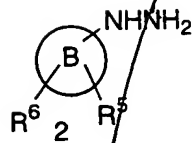
36. A process for preparing a compound of Formula (I) selected from compounds of Claim 1, which process comprises:

(i) reacting a 2-keto-3-phenylaminoacrylonitrile of Formula 1:

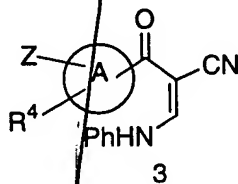


with a hydrazine of Formula 2:

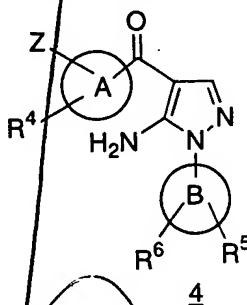




- where  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are as defined in Claim 1 to provide a compound of Formula (I) where  $R^1$  is hydrogen; or
- (ii) reacting a 2-keto-3-phenylaminoacrylonitrile of formula 3:



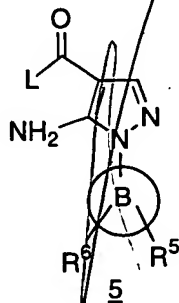
- where Z is either hydroxy, nitro or halo group and  $R^4$  are as defined in Claim 1 with a hydrazine of formula 2 to provide a compound of formula 4:



followed by conversion of the Z group to the desired  $R^3$  group to provide a compound of Formula (I) where  $R^1$  is hydrogen;

- (iii) optionally modifying any of the  $R^1$ ,  $R^3$ ,  $R^4$ ,  $R^5$  or  $R^6$  groups;
- (iv) optionally converting the compound of Formula (I) prepared in Steps (i), (ii) or (iii) above, to the corresponding acid addition salt by treatment with an acid;
- (v) optionally converting the compound of Formula (I) prepared in Steps (i), (ii) or (iii) above, to the corresponding free base by treatment with a base; and
- (vi) optionally separating a mixture of stereoisomers of a compound of Formula (I) prepared in Steps (i) - (v) above, to give a single stereoisomer.

37. A process for preparing a compound of Formula (I) selected from compounds of Claim 1, which process comprises reacting a compound of Formula 5:



where L is a leaving group under organometallic displacement reaction conditions

with an organometallic reagent of formula where M is a metallic moiety to provide a compound of Formula (I) where R<sup>1</sup> is hydrogen;

- (ii) optionally modifying any of the R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> or R<sup>6</sup> groups;
- (iii) optionally converting the compound of Formula (I) prepared in Steps (i) or (ii) above, to the corresponding acid addition salt by treatment with an acid;
- (iv) optionally converting the compound of Formula (I) prepared in Steps (i) or (ii) above, to the corresponding free base by treatment with a base; and
- (v) optionally separating a mixture of stereoisomers of a compound of Formula (I) prepared in Steps (i) or (iv) above, to give a single stereoisomer.

\* ... \* ... \* ... \*